Allergy and contrast media

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Key words: allergy; anaphylaxis; contrast media; immediate hypersensibility.

• The allergic origin of severe reactions following the injection of iodinated contrast media (ICM) is disputed. However, three publications argue that immediate hypersensitivity is probably due to IgE mediation (1–3). The description of clinical signs and measurement of mediators (histamine, tryptase) play an important role since cutaneous tests and specific IgEs are not validated for ICMs.

Five cases of severe anaphylactoid reactions.

We report five clinical cases of severe reactions (including one death) occurring after an intra-arterial injection of the same ionic ICM in three patients and two nonionic ICMs in two other patients (Table 1). The clinical symptoms corresponded in each case to the grade III (4) minimum. All the patients had been in contact with the culprit ICM at least once (prior exposure). Treatment with intravenous epinephrine was successful in four cases. One patient died from cardiovascular collapse followed by multiorgan failure 16 h after the injection.

Measurement of mediators (histamine and tryptase) was done. After the patients gave informed consent, prick tests and intradermal tests (IDT) were carried out 6 weeks after the incident to identify the culprit ICM. A prick test with pure ICM on the forearm, is positive if 15 min later a wheal appears which is equal to at least half the positive control (using an extract of codeine phosphate at 9%) and larger than the negative control (saline solution). An IDT is done on the patient's back by injecting 0.15 ml of ICM at a concentration ranging from 10^{-3} to 10^{-1}, raising a bleb of about 3 mm. The IDT is positive if 15 min

Table 1.

Patient no.	1	2	3	4	5
Sex/age (years)	M/61	M/61	F/80	M/78	M/72
ICM	Ioxaglate*	Ioxaglate	Ioxaglate	Iopromide**	Iopentol†
Procedure	Arteriography	Arteriography	Coronary angioplasty	Arteriography	Arteriography
Time lapse (in min)					
after injection	30	Immediate	Immediate	10	30
Grade	III	III	IV	III	III
Cut	+	+	+	+	+
BS				+	
AP	↘	↘	↘	↘	↘
HR	→	↗	Ventricular arrhythmia	↗	→
Treatment	Epinephrine	Epinephrine	Epinephrine, cardiac massage, defibrillation	Epinephrine	Epinephrine
Evolution	Recovery	Recovery	Death	Recovery	Recovery
Premedication	Hydroxyzine	0	0	Hydroxyzine	Hydroxyzine
Prior exposure	I/II after ICM 5 years earlier	I/II with ICM 2 years earlier	II after injection 10 days earlier	1 month earlier: no incident	1 month earlier no incident
Allergologic assessment					
Histamine (Immunotech, Luminy, France)	ND	ND	>400	66.7	ND
Tryptase (UniCAP, Pharmacia, Sweden)	ND	36	>200	38	39.7
IDT	Ioxaglate $\oplus$ 10^{-1} (3→6 mm)	Ioxaglate $\oplus$ 10^{-2} (3→9 mm)	–	Iopromide $\oplus$ 10^{-2} (3→6 mm)	Iopentol $\oplus$ 10^{-2} (3→9 mm)
Cross-reactivity	–	$\oplus 10^{-1}$ ioxitalamate††	–	–	$\oplus$ 10^{-1} iomeprol†††

There were 10 negative controls for each ICM.
* (HEXABRIX®).
** (ULTRAVIST®).
† (IVEPAQUE®).
†† (TELEBRIX®).
††† (IOMERON®).
Cut: cutaneous; BS: bronchospasm; AP: arterial pressure (mmHg); HR: heart rate ($b.min^{-1}$).

after the injection, there is a wheal at least double the size of the injection bleb, and which shows signs of erythema surrounded by flare. The IDT is compared to a positive control (codeine phosphate: 50 μg/ml) and a negative control (saline solution).

In our subjects, the rate of the mediators had increased. The prick tests to ICMs were 50% negative, whereas the IDTs were positive every time (Table 1).

The severity of and time lapse in the onset of clinical signs, prior exposure, increase in tryptase level which seemed to be correlated to the severity of the reaction (3), positivity of IDTs, and reintroduction of a nonreactive ICM in cutaneous tests without incident all support the hypothesis of IgE mediation. Thus, cutaneous tests appear to be of prime importance in identifying the culprit ICM. ICMs are viscous and spread with difficulty into the epidermis. This may explain the negativity of prick tests. On the other hand, IDTs seem to be more appropriate for a reaction that provokes every time a wheal at least double the injection wheal.

However, this test is positive according to the degree of sensitivity of each patient: the more the patient is sensitized, the weaker the reactive concentration is. The test starts at 10^{-3} and goes to 10^{-1}, a concentration that does not produce histamine release, even with hyperosmolar ICMs, as proved by negative IDTs at 10^{-1} for ioxitalamate (Telebrix®) in nonallergic patients who presented an incident of mild severity to this ICM (1).

Therefore, we suggest that patients who have had an anaphylactoid reaction to an ICM injection should have their tryptase level measured (considered as the marker of mast-cell activation) (5) and should undergo intradermal tests so as to identify and eliminate the culprit ICM in order to avoid any subsequent allergic accidents. Searching for cross-sensitization seems to be necessary. In two cases, this has enabled us to determine to which ICMs the patients were not sensitized and to inject them with these safely.

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Exhaled NO reduced on allergen avoidance

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Key words: allergen avoidance; mite; nitric oxide.

• In a previous study (1), we have shown that the level of exhaled nitric oxide (NO) (ENO) represents a sensitive and promptly modifiable marker to monitor antigen exposure in mite-sensitized asthmatic children. This study aimed to determine whether the actual level of exposure to house-dust-mite (HDM) antigen can influence the magnitude of ENO reduction after antigen avoidance in a group of allergic asthmatic children.

NO reduction is related to starting exposure level.

We evaluated the level of ENO before (T0) and after a 3-month period of mite avoidance (T1) in an Alpine environment (Misurina, Italian Dolomites; altitude: 1756 m) in a group of 14 schoolchildren sensitized to HDM. The level of HDM group I antigen from the beds of the patients in their family homes was measured by a two-site immunometric ELISA (2). Exhaled NO measurements were made with a chemiluminescence analyzer (Logan LR 2149, Rochester, UK) (3). Values of ENO considered in the data analysis were always measured in the last part of exhalation (plateau of exhaled NO), taking the plateau of the end-exhaled CO_2 reading as representative of an alveolar sample (3).

None of the children in this group had presented airway tract infection for at least 1 month before each of the NO measurements. None of them were allergic to furred pets.

The children had received a regular course of inhaled steroids for at least 3 months at